T-cell-potentiating melanoma therapy

Metastatic melanoma patients face rising death rates and bleak survival estimates for distant metastases, and therapy involves enrollment in a clinical trial as the standard of care. Thus, Hodi and colleagues conducted a randomized double-blind 676-patient phase III study to examine the efficacy of ipilimumab, a monoclonal antibody that blocks cytotoxic T-lymphocyte-associated antigen 4, in combination with a glycoprotein 100 (gp100) peptide vaccine and to compare the treatment with administration of gp100 alone. Treatment with ipilimumab both with and without gp100, as compared with gp100 alone, improved overall survival in metastatic melanoma patients who had undergone previous therapy, indicating that ipilimumab efficacy was not improved by gp100 administration. Reported adverse effects, most notably immune-related events such as diarrhea, may be treatment limiting. Taken together, these results indicate that ipilimumab may be useful as a treatment for metastatic melanoma patients who experienced disease progression following previous therapies. (*N Engl J Med* 363:711–23, 2010) *Selected by T. Schwarz*

Risky adolescence

Studies of increased risk of melanoma following sunbed use have typically recruited people with melanoma diagnosed at any age. Thus, the specific associations between sunbed use and melanoma in young adults are not known. This relationship is particularly intriguing because younger people may have a greater susceptibility to the carcinogenic effects of artificial UV light. In an analysis of a population-based case–control family study of early-onset melanoma in Australia, Cust and colleagues demonstrated that sunbed use is a risk factor for early-onset (between ages 18 and 39) melanoma. Moreover, evidence of a dose–response relationship between the number of tanning bed sessions and melanoma risk was found in this population. The risk of melanoma was greater with earlier age of first sunbed use and for earlier onset disease. Because sunbed use was found to cause 76% of melanomas in 18- to 29-year-olds who have ever used a sunbed, efforts to restrict minors and discourage young adults from sunbed use should be intensified. (*Int J Cancer*, published online 28 July 2010; doi:10.1002/ijc25576, 2010) *Selected by M. Weinstock*

Detrimental healing

Although Aqueous Cream BP is a widely used emollient for the treatment of dry skin and eczema, adverse cutaneous reactions occur frequently with use. These reactions may stem from the preservative chlorocresol, the antiseptic phenoxyethanol, or the anionic surfactant sodium lauryl sulfate (SLS). To examine the effects of this emollient on the skin barrier *in vivo*, Tsang and Guy examined the repeated, short-term application of this agent to forearm skin in six healthy female volunteers. Interestingly, this application led to a significant reduction in stratum corneum thickness and an overall increase in baseline transepidermal water loss. Based on the composition of the emollient's formulation, the authors concluded that SLS, an amphiphilic surfactant used for its solubilizing, suspension, and emulsifying properties, is the most likely culprit for these detrimental reactions. The observed results for healthy skin indicate that use of Aqueous Cream BP to treat eczema should be reconsidered because the barrier function of eczematous skin may already be compromised. (*Br J Dermatol* 163:954–8, 2010) *Selected by H. Williams*

News on the forefront of psoriasis

Genome-wide association studies (GWAS) have implicated several genomic regions (*PSORS1*, *IL12B*, *IL23R*, *IL4-IL13*, *IL23A*, *TNIP1*, *TRNFIP3*, *LCE3B-LCE3C*, *DEFB4*, and *SPATA2-RNF114*) in the pathogenesis of psoriasis; however, these genetic loci do not account for the observed variability in genetic susceptibility to this disease, indicating that other genetic factors remain unknown. Recently, three publications in *Nature Genetics* presented GWAS analyses that revealed new psoriasis susceptibility loci. Ellinghaus and colleagues performed genome-wide single-nucleotide polymorphism analysis of 487 German psoriasis vulgaris cases and 1,161 controls. *TRAF3IP2* on 6q21, which encodes the TRAF-interacting protein 2, was identified as a psoriasis-susceptibility locus. Stuart and colleagues similarly performed a meta-analysis of recent GWAS that examined 4,064 cases and 4,685 controls from the United States, Canada, and Germany. These analyses uncovered three new susceptibility loci at *NOS2*, which encodes inducible nitric oxide synthase: *FBXL19*, which encodes an inhibitor of NFκ light-chain enhancer of activated B cells (NF-κB); and *PSMA6-NFKBIA*, which encodes an inhibitor of NF-κB signaling and a subunit involved in major histocompatibility complex class I antigen processing, as well as confirming the recently reported association near *RNF114*.

Finally, Sun and colleagues extended their previous GWAS in the Chinese population and compared their results with studies from Germany and the United States. This study identified six new susceptibility loci associated with psoriasis and also confirmed one previously identified locus (*TNIP1-ANZA6*). Several of the newly identified loci (*ERAP1*, *PTTG1*, *CSMD1*, *GJB2*, *SERPINB8*, and *ZNF816A*) have been implicated in other autoimmune diseases. Interestingly, all six loci demonstrated significant heterogeneity between the Chinese samples and the European samples.

Taken together, these studies underscore the importance of the immune system in psoriasis and highlight new potential biological pathways involved in this chronic immune-mediated skin disease. (*Nat Genet* 42:991–5, 2010; *Nat Genet* 42:1000–4, 2010; *Nat Genet* 42:1005–9, 2010) *Selected by T. Schwarz*

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